Migraine Pharmacotherapy

Based on the American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice (2021)

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Acute Treatment

Acute Treatment Goals

- Achieve fast relief and freedom from symptoms
- Achieve functional recovery
- Minimize need for additional doses or medications
- Optimize of self-care and reduce need for resources
- Minimize adverse events
- Maintain cost-effective management

Important Considerations

- Individualized **lifestyle modifications** are important
- Acute treatment should be offered to **all patients** with confirmed migraine diagnosis
- Use acute treatment medications at the onset of attack, **at the first sign of pain**

Acute Treatment Options

Migraine-specific Agents

Established efficacy	Probably effective
• **Triptans** *(e.g., sumatriptan, rizatriptan, zolmitriptan)* • Ergotamine derivatives *(e.g., **dihydroergotamine**)* • Small molecule CGRP receptor antagonists *("**gepants**"; e.g., rimegepant, ubrogepant, zavegepant)* • Selective serotonin receptor agonist *(e.g., **lasmiditan**)*	• Ergotamine • Other forms of dihydroergotamine

Non-specific Agents

Established efficacy	Probably effective
• **NSAIDs** (*aspirin, diclofenac, ibuprofen, naproxen, celecoxib oral solution*) • Combination analgesic: ***(acetaminophen/aspirin/caffeine)***	• NSAIDs *(flurbiprofen, ketoprofen, IV or IM ketorolac)* • IV magnesium *(in migraine with aura)* • Isometheptene-containing compounds • Antiemetics *(chlorpromazine, droperidol, metoclopramide, prochlorperazine, promethazine)*

Acute Treatment Recommendations

Mild to moderate attacks
Non-specific agents recommended

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Inadequate response to non-specific agents

→ **Triptan***

↓

Inadequate response to initial treatment

← **Second triptan**

↓

Criteria for initiating small molecule CGRP receptor antagonists, lasmiditan, or neuromodulatory devices

- Prescribed/recommended by a licensed clinician for an adult patient
- ICHD-3 diagnosis of migraine (with aura, without aura, or chronic)
- Either of the following regarding triptans:
  (1) Triptans are either contraindicated or not tolerated
  (2) Inadequate response to at least **two** oral triptans (per clinician's attestation or patient-reported outcome questionnaire)

↓

Small molecule CGRP receptor antagonists, lasmiditan, or neuromodulatory devices

Moderate to severe attacks
Migraine-specific agents recommended

↓

Triptan*

*Triptans are generally considered the first-line migraine-specific options; non-oral options such as dihydroergotamine may be considered for patients for whom traditional oral options are inappropriate (e.g., those with severe nausea/vomiting)

Preventive Treatment

Preventive Treatment Goals

- Reduce attack frequency, severity, and duration
- Reduce disability associated with migraine attacks
- Improve treatment response, prevent escalation
- Improve function
- Reduce need for intolerable, ineffective, unwanted acute treatment
- Reduce overall cost of migraine treatment
- Provide sense of control; allow self-management
- Improve health-related quality of life
- Reduce psychological burdens of migraine

When to Consider Preventive Treatment

Consider preventive treatment in **any** of these situations

- Significant interference in daily life from migraine attacks despite acute treatment
- **Frequent attacks****
- Contraindication to acute treatments or failure of acute treatments
- Adverse effects associated with acute treatment
- **Overuse**** of acute treatments
- Patient preference
- Certain uncommon migraine types (e.g., brainstem or prolonged aura)
- History of migrainous infarction (regardless of attack frequency)

**Definitions

Frequent attacks (for prevention criteria)

Offer preventive treatment if:

- ≥ 6 MHD, even if they cause no disability
- ≥ 4 MHD, if they cause some disability
- ≥ 3 MHD, if they cause severe disability

Consider preventive treatment if:

- 4 or 5 MHD with no disability
- 3 MHD with some disability
- 2 MHD with severe disability

Overuse (for prevention criteria)

- ≥ 10 days/month for ergot derivatives, triptans, opioids, combination analgesics, and a combination of drugs from different classes that are not individually overused
- ≥ 15 days/month for nonopioid analgesics, acetaminophen, and NSAIDs

Adequate trials

- Oral agents: at least **8 weeks** at target therapeutic dose
  - Patients with partial response may experience additional benefit over 6-12 months
- Parenteral CGRP mAbs:
  - At least **3 months** (if administered monthly)
  - At least **6 months** (if administered quarterly)

Preventive Treatment Options

Oral Agents

Established efficacy	Probably effective
• Candesartan • Antiepileptics *(divalproex sodium, valproate sodium, topiramate)* • Beta blockers *(metoprolol, propranolol, timolol)* • CGRP receptor antagonists *(rimegepant, atogepant)*	• Lisinopril • Antidepressants (amitriptyline, venlafaxine) • Beta blockers (atenolol, nadolol) • Memantine

Parenteral Agents

Established efficacy	Probably effective
• CGRP mAbs *(eptinezumab, erenumab, fremanezumab, galcanezumab)* • OnabotulinumtoxinA	• OnabotulinumtoxinA + CGRP mAb

Initiating CGRP mAbs

The guideline recommends that CGRP mAbs be considered for preventive treatment in a patient **18 years or older** if any of the three conditions to the right are met.

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1. ICHD-3 diagnosis of migraine (with or without aura), **4-7 MMD**, and **both** of the following:
- Intolerability/inadequate response to an 8-week trial** of two or more of the preventive options listed above
- At least moderate disability

2. ICHD-3 diagnosis of migraine (with or without aura), **8-14 MMD** and intolerability/inadequate response to an 8-week trial** of two or more of the preventive options listed above

3. ICHD-3 diagnosis of **chronic** migraine and **either** of the following:
- Intolerability/inadequate response to an 8-week trial** of two or more of the preventive options listed above
- Intolerability or inadequate response to at least 2 quarterly injections of onabotulinumtoxinA

Reference: Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. Headache. 2021;61(7):1021-1039. doi:10.1111/head.14153

Abbreviations

CGRP calcitonin gene-related peptide
ICHD-3 International Classification of Headache Disorders, 3rd edition
MHD monthly headache days
MMD monthly migraine days

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